DPYS gene

dihydropyrimidinase

Normal Function

The *DPYS* gene provides instructions for making an enzyme called dihydropyrimidinase. This enzyme is involved in the breakdown of molecules called pyrimidines, which are building blocks of DNA and its chemical cousin RNA. The dihydropyrimidinase enzyme is involved in the second step of the three-step process that breaks down pyrimidines. This step opens the ring-like structures of molecules called 5,6-dihydrothymine and 5,6-dihydrouracil. Further breakdown of these molecules leads to the production of other molecules called beta-aminoisobutyric acid and beta-alanine, which are thought to play roles in the nervous system. Beta-aminoisobutyric acid increases the production and release (secretion) of a protein called leptin, which has been found to help protect brain cells from damage caused by toxins, inflammation, and other factors. Beta-alanine is thought to be involved in sending signals between nerve cells (synaptic transmission) and in controlling the level of a chemical messenger (neurotransmitter) called dopamine.

The dihydropyrimidinase enzyme also helps break down certain drugs called fluoropyrimidines that are used to treat cancer. Common examples of these drugs are 5-fluorouracil and capecitabine.

Health Conditions Related to Genetic Changes

dihydropyrimidinase deficiency

At least 23 *DPYS* gene mutations have been identified in people with dihydropyrimidinase deficiency, a disorder that can cause neurological and gastrointestinal problems in some affected individuals. Other people with dihydropyrimidinase deficiency have no signs or symptoms related to the disorder, and in these individuals the condition can be diagnosed only by laboratory testing. People with dihydropyrimidinase deficiency, including those who otherwise exhibit no symptoms, may be vulnerable to severe, potentially life-threatening toxic reactions to fluoropyrimidines. These drugs may not be broken down efficiently and can build up to toxic levels in the body (fluoropyrimidine toxicity), leading to drug reactions including gastrointestinal problems, blood abnormalities, and other signs and symptoms.

The *DPYS* gene mutations that cause dihydropyrimidinase deficiency greatly reduce or eliminate dihydropyrimidinase enzyme function. As a result, the enzyme is unable to begin the breakdown of 5,6-dihydrothymine and 5,6-dihydrouracil. Excessive

amounts of these molecules accumulate in the blood and in the fluid that surrounds and protects the brain and spinal cord (the cerebrospinal fluid or CSF) and are released in the urine.

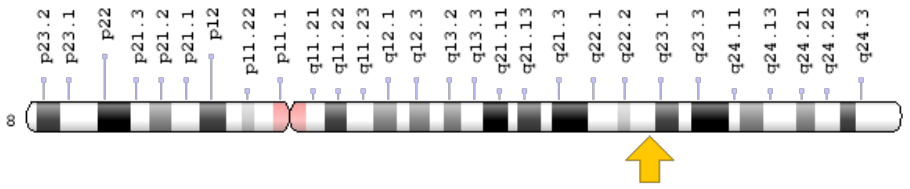
The relationship between the inability to break down 5,6-dihydrothymine and 5,6-dihydrouracil and the specific features of dihydropyrimidinase deficiency is unclear. Failure to complete this step in the breakdown of pyrimidines also impedes the final step of the process, which produces beta-aminoisobutyric acid and beta-alanine. Reduced production of these molecules may impair their function in the nervous system, leading to neurological problems in some people with dihydropyrimidinase deficiency. Because fluoropyrimidine drugs are broken down by the same three-step process as pyrimidines, deficiency of the dihydropyrimidinase enzyme can lead to the drug buildup that causes fluoropyrimidine toxicity.

It is unknown why some people with dihydropyrimidinase deficiency do not develop health problems related to the condition; other genetic and environmental factors likely help determine the effects of this disorder.

Chromosomal Location

Cytogenetic Location: 8q22.3, which is the long (q) arm of chromosome 8 at position 22.3

Molecular Location: base pairs 104,379,424 to 104,467,075 on chromosome 8 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DHP
- DHPase
- dihydropyrimidine amidohydrolase
- hydantoinase

Additional Information & Resources

Educational Resources

- NetBioChem: Pyrimidine Catabolism
  http://library.med.utah.edu/NetBiochem/pupyr/pp.htm#Py%20Catab

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28DPYS%5BTIAB%5D%29+OR+%28dihydropyrimidinase%5BTIAB%5D%29%29+OR+%28%28DHP%5BTIAB%5D%29+OR+%28DHPase%5BTIAB%5D%29+OR+%28hydantoinase%5BTIAB%5D%29+OR+%28dihydropyrimidine+amidohydrolase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- DIHYDROPYRIMIDINASE
  http://omim.org/entry/613326

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_DPYS.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=DPYS%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=3013
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/1807
- UniProt
  http://www.uniprot.org/uniprot/Q14117

Sources for This Summary

- OMIM: DIHYDROPYRIMIDINASE
  http://omim.org/entry/613326
- Hamajima N, Kouwaki M, Vreken P, Matsuda K, Sumi S, Imaeda M, Ohba S, Kidouchi K, Nonaka M, Sasaki M, Tamaki N, Endo Y, De Abreu R, Rotteveel J, van Kuilenburg A, van Gennip A, Togari H, Wada Y. Dihydropyrimidinase deficiency: structural organization, chromosomal localization, and mutation analysis of the human dihydropyrimidinase gene. Am J Hum Genet. 1998 Sep;63(3): 717-26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9718352
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1377410/
- Schnackerz KD, Dobritzsch D. Amidohydrolases of the reductive pyrimidine catabolic pathway purification, characterization, structure, reaction mechanisms and enzyme deficiency. Biochim Biophys Acta. 2008 Mar;1784(3):431-44. doi: 10.1016/j.bbapap.2008.01.005. Epub 2008 Jan 18. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18261476
- Sumi S, Imaeda M, Kidouchi K, Ohba S, Hamajima N, Kodama K, Togari H, Wada Y. Population and family studies of dihydropyrimidinuria: prevalence, inheritance mode, and risk of fluorouracil toxicity. Am J Med Genet. 1998 Jul 24;78(4):336-40.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9714435
- van Kuilenburg AB, Dobritzsch D, Meijer J, Meinsma R, Benoist JF, Assmann B, Schubert S, Hoffmann GF, Duran M, de Vries MC, Kurlemann G, Eyskens FJ, Greed L, Sass JO, Schwab KO, Sewell AC, Walter J, Hahn A, Zoetekouw L, Ribes A, Lind S, Hennekam RC. Dihydropyrimidinase deficiency: Phenotype, genotype and structural consequences in 17 patients. Biochim Biophys Acta. 2010 Jul-Aug;1802(7-8):639-48. doi: 10.1016/j.bbadis.2010.03.013. Epub 2010 Apr 1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20362666
- van Kuilenburg AB, Meijer J, Dobritzsch D, Meinsma R, Duran M, Lohkamp B, Zoetekouw L, Abeling NG, van Tinteren HL, Bosch AM. Clinical, biochemical and genetic findings in two siblings with a dihydropyrimidinase deficiency. Mol Genet Metab. 2007 Jun;91(2):157-64. Epub 2007 Mar 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17383919
- van Kuilenburg AB, Meinsma R, Zonnenberg BA, Zoetekouw L, Baas F, Matsuda K, Tamaki N, van Gennip AH. Dihydropyrimidinase deficiency and severe 5-fluorouracil toxicity. Clin Cancer Res. 2003 Oct 1;9(12):4363-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14555507

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